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09/941,769	08/30/2001	Atsumu Hirabayashi	1021.40593X00	7364

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EXAMINER

CHAKRABARTI, ARUN K

ART UNIT PAPER NUMBER

1634

DATE MAILED: 03/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.
09/941,769

Applicant(s)
Hirabayashi

Examiner
Arun Chakrabarti

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1634



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Jan 17, 2003
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-20 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____ 6) ☒ Other: **Detailed Action**

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DETAILED ACTION

Specification

1. Claims 1-4, and 8-12 have been amended. New claims 13-20 have been added.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 4, and 13-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for weighting factors 1 and 2 (w(1), and w(2)) as disclosed on page 21 of the specification), does not reasonably provide enablement for any number w(n). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The Court in *re Wands*, 8 USPQ2d 1400 (CA FC 1988) stated with regard to enablement that

“Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman*. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and

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(8) the breadth of the claims.”

Here, the claim is broadly drawn to a method of any DNA analysis by calculating any $S(I)$ value using any weighting factor $W(n)$. However, the specification does not provide guidance commensurate in scope with this claim, teaching only two numbers $w(1)$ and $w(2)$. Specification provides minimal guidance regarding method of detecting the effectiveness of the analysis. There is no working example of such testing. It is highly unpredictable whether or what other detection method would function in the context of method of detecting the effectiveness of analysis of any mass spectrum. This unpredictability is borne out of the fact that if the number T increases more than 4, the contamination of the sample arises (as disclosed in the specification, page 21, lines 9-12). Further, each type of unknown polymorphism has unpredictable effects on mass spectrometric profile, and no general method for polymorphism detection is presented. It would require a large amount of experimentation, potentially including the testing of detection method in millions of nucleic acid polymorphisms, in order to identify additional sampling means with the claimed functionality. Given the Wand's factors opposing the full scope of enablement including the limited teaching in the specification, the absence of any working example without any S.E.M. value to determine the degree of significance (p-value as usually determined by Student's t-test), the unpredictability of the art, the breadth of the claim, and the large amount of experimentation needed, with only the skill level in the art being neutral towards enablement, it is concluded that undue experimentation is necessary to make and use the invention as broadly claimed.

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4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-20 are rejected under 35 U.S.C. 112 (2nd paragraph) for failing to distinctly claim the subject matter which the applicant regards as his invention.

Regarding claim 1, the phrase "including" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention.

Claim 4, and 13-20 are vague and indefinite over the recitation of the phrase, "level of influence" on line 9. It is not clear how measuring of one sample is influencing the measurement of another sample at different time. Is the same cuvette or assay location being used for the measurement of several samples consecutively? If not, what kind of influence is claimed? Is the biological influence claimed, or physical influence claimed, or chemical influence claimed, or all of them are claimed? The metes and bounds of the claim are vague and indefinite.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1-3, and 5-6 are rejected under 35 U.S.C. 102 (b) as being anticipated by Koster (U.S. Patent 5,605,798) (February 25, 1997).

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Koster teaches a DNA analysis system for analysis system for analyzing DNA polymorphism (Abstract), comprising:

a) ionization means for generating plural kinds of multiply-charged ions of a test DNA fragment, where each of them has five or more charges (Example 2, Figures 11B and C, Column 2, lines 46-61, and Column 11, lines 2-10);

b) mass spectrometric means for performing a mass spectrometry on the multiply-charged ion formed by the ionization means (Example 2, Figures 11B and C, and Column 11, line 2 to Column 12, line 23);

c) analyzing-result prediction means that predicts a mass spectrum pattern from the mass spectrometric means in each of two cases, where one is that the test DNA fragment is polymorphic and the other is that the test DNA fragment is not polymorphic, based on both information about the test DNA fragment and information about a polymorphism point (Figure 1C);

d) comparative processing means for comparing a plurality of the mass spectrum patterns predicted by the analyzing-result prediction means with the analyzing results of the test DNA fragment analyzed by the mass spectrometric means to determine a nucleic acid base on the polymorphism point (Figure 1c, 2-3, and Figure 11, and Column 11, line 10 to column 12, line 23).

Koster teaches a DNA analysis system, wherein the analyzing-result prediction means predicts a mass-to-charge ratio (m/z ; m is an ion mass, z is the number of electric charges) of the

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plural kinds of multi-charged ions and a distribution of ion intensities in each of two cases, where one is that the test DNA fragment is polymorphic and the other is that the test DNA fragment is not polymorphic (Figure 1C).

Koster inherently teaches a DNA analysis system, further comprising:

a) sampling means for supplying a sample including test DNA fragments to the ionization means at fixed intervals (Example 2); (the inference is deduced from the fact that any electrospray mass spectrometer, as taught by Koster, essentially contains a sampling means for supplying a sample at fixed intervals);

b) detecting-output analysis means for subtracting a mass spectrum obtained as an analyzing result with respect to a sample previously measured and modified by weight from a mass spectrum obtained as a detecting-output of the mass spectrometric means (Example 2, and Figure 11), wherein

the mass spectrum processed by the detecting-output analysis means is provided as an analyzing result with respect to the test DNA fragment in the sample (Figure 1C).

Koster teaches a DNA analysis system, wherein the ionization means generates multiply-charged ions of the test DNA fragment by the ionization means using an air atomization (Example 2 and Column 2, line 45 to Column 3, line 14).

Koster teaches a DNA analysis system, wherein a nucleic acid base of a single nucleotide polymorphism point in the test DNA fragment is specified (Column 10, line 46 to Column 12, line 30).

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Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 7-10 are rejected under 35 U.S.C. 103 (a) over Koster (U.S. Patent 5,605,798) (February 25, 1997) in view of Haff et al (U.S. Patent 5,885,775) (March 23, 1999).

Koster teaches the DNA analysis system of claims 1-3, and 5-6 as described above including the plurality of measurement systems, where each of the measurement systems comprises the sampling means, the ionization means, and the mass spectrometric means (Figures 6B and 6C, and Column 9, lines 27-42) as well as on-line data transfer to a computer (Column 2, lines 33-40).

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Koster does not teach the DNA analysis system comprising display means for displaying the occurrence of an emergency when a maximum ion intensity detected by the mass spectrometric means is smaller than a predetermined threshold and communication means for sending information about the occurrence of the emergency to a system administrator.

Haff et al teach the display means for displaying the occurrence of an emergency when a maximum ion intensity detected by the mass spectrometric means is smaller than a predetermined threshold and communication means for sending information about the occurrence of the emergency to a system administrator (Column 6, lines 40-60 and Figure 14).

Koster does not teach the DNA analysis system when a maximum ion intensity of a mass spectrum of the standard sample detected by the mass spectrometric means is equal to or higher than the threshold, the sample where the maximum ion intensity of the mass spectrum is detected as one smaller than the threshold is re-supplied to the ionization means by the sampling means.

Haff et al teach the DNA analysis system when a maximum ion intensity of a mass spectrum of the standard sample detected by the mass spectrometric means is equal to or higher than the threshold, the sample where the maximum ion intensity of the mass spectrum is detected as one smaller than the threshold is re-supplied to the ionization means by the sampling means (Column 6, lines 40-60 and Figure 14).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the display means for displaying the occurrence of an emergency when a maximum ion intensity detected by the mass spectrometric means is

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smaller than a predetermined threshold and communication means for sending information about the occurrence of the emergency to a system administrator of Haff et al. in the method of Koster, since Haff et al state, "The present invention relates to a method for quickly determining polynucleotide sequences, with low labor intensity and low cost per SNP assay (Column 1, lines 44-46)." By employing scientific reasoning, an ordinary practitioner would have been motivated to combine and substitute the display means for displaying the occurrence of an emergency when a maximum ion intensity detected by the mass spectrometric means is smaller than a predetermined threshold and communication means for sending information about the occurrence of the emergency to a system administrator of Haff et al. in the method of Koster in order to improve the process for determining polynucleotide sequences and also in order to achieve the express advantages, as noted by Holtzman, of an invention which relates to a method for quickly determining polynucleotide sequences, with low labor intensity and low cost per SNP assay.

7. Claims 11, and 12 are rejected under 35 U.S.C. 103 (a) over Koster (U.S. Patent 5,605,798) (February 25, 1997) in view of Haff et al (U.S. Patent 5,885,775) (March 23, 1999) further in view of Harris et al. (U.S. Patent 4,353,242) (October 12, 1982).

Koster in view of Haff et al teach the DNA analysis system of claims 7-10 as described above.

Koster in view of Haff et al do not teach the system wherein the occurrence of the emergency information is transmitted to sampling means of another measurement systems.

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Harris et al. teach the analysis system, wherein the occurrence of the emergency information is transmitted to sampling means of another measurement systems (Column 8, lines 8-19).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the analysis system, wherein the occurrence of the emergency information is transmitted to sampling means of another measurement system of Harris et al in the method of Koster in view of Haff et al, since Harris et al state, "A computer is typically used as a backup with all such combined systems to tie everything together (Column 8, lines 15-17)." By employing scientific reasoning, an ordinary practitioner would have been motivated to combine and substitute the analysis system, wherein the occurrence of the emergency information is transmitted to sampling means of another measurement system (e.g., another computer) of Harris et al in the method of Koster in view of Haff et al in order to improve the process for determining polynucleotide sequences and also in order to achieve the express advantages, as noted by Harris et al, of an invention which provides a computer that is typically used as a backup with all such combined systems to tie everything together.

Response to Amendment

8. In response to amendment, a new 112 (first and second paragraph) rejection have been included. All previous 102 and 103(a) rejections have been properly maintained.

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Response to Arguments

9. Applicant's arguments filed on January 17, 2003 have been fully considered but they are not persuasive.

Applicant argues that 102(b) rejection should be withdrawn because Koster reference does not teach "generation of plural kind of multiple charged ions". This argument is not persuasive. Koster explicitly teaches "generation of plural kind of multiple charged ions", as Koster states, "The generation of multiple ion peaks which can be obtained using ES mass spectrometry can increase the accuracy of the mass determination" (Column 11, lines 6-8).

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Applicant also argues that there is no motivation to combine the references. This argument is not persuasive, especially in the presence of strong motivation provided by Haff et al. since Haff et al. state, "The present invention relates to a method for quickly determining polynucleotide sequences, with low labor intensity and low cost per SNP assay (Column 1, lines 44-46)." The same logic is applicable to other references as well.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into

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account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Applicant then argues the 103 rejection is improper because it is "obvious to try" and lacks a reasonable expectation of success.

With regard to the "obvious to try" argument, The MPEP 2143.02 states "Obviousness does not require absolute predictability, however, at least some degree of predictability is required. Evidence showing there was no reasonable expectation of success may support a conclusion of nonobviousness. *In re Rinehart*, 531 F.2d 1048, 189 USPQ 143 (CCPA 1976) (Claims directed to a method for the commercial scale production of polyesters in the presence of a solvent at superatmospheric pressure were rejected as obvious over a reference which taught the claimed method at atmospheric pressure in view of a reference which taught the claimed process except for the presence of a solvent. The court reversed, finding there was no reasonable expectation that a process combining the prior art steps could be successfully scaled up in view of unchallenged evidence showing that the prior art processes individually could not be commercially scaled up successfully.). See also *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir.), cert. denied, 502 U.S. 856 (1991) (In the context of a biotechnology case, testimony supported the conclusion that the references did not show that there was a reasonable expectation of success. 18 USPQ2d at 1022, 1023.); *In re O'Farrell*, 853

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F.2d 894, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988) (The court held the claimed method would have been obvious over the prior art relied upon because one reference contained a detailed enabling methodology, a suggestion to modify the prior art to produce the claimed invention, and evidence suggesting the modification would be successful.).”

There is no evidence of record submitted by applicant demonstrating the absence of a reasonable expectation of success. There is evidence in the Koster reference of the enabling methodology, the suggestion to modify the prior art, and evidence that a number of different genetic diseases or chromosomal abnormalities, a predisposition to a disease or infection by a pathogenic organism were actually experimentally studied and found to be functional (Abstract and Claim 18). This evidence of functionality trumps the attorney arguments, which argues that Koster reference is an invitation to research, since Koster steps beyond research and shows the functional product.

In view of the response to arguments, all previous 102(b) and 103(a) rejections have been maintained properly.

Conclusion

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph.D., whose telephone number is (703) 306-5818. The examiner can normally be reached on 7:00 AM-4:30 PM from Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703) 308-1119. The fax phone number for this Group is (703) 746-4979.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group analyst Chantae Dessau whose telephone number is (703) 605-1237.

Arun Chakrabarti,
Patent Examiner,

Application/Control Number: 09/941,769

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March 5, 2003


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